Reviewer’s report

Title: Patients' beliefs towards informed consent in low-risk pragmatic trials

Version: 0 Date: 30 Jul 2017

Reviewer: Stephanie Kraft

Reviewer’s report:

The goal of this manuscript, i.e. to understand how patients with a chronic condition view various approaches to informed consent for low-risk pragmatic trials, is an important one. However, I have a number of concerns about the framing and interpretation of this manuscript, primarily related to the focus on the hypertension population. First, it is not clear whether this population was looked at because of the potential implications of having any chronic condition vs. having hypertension and therefore being familiar with the specific medications described in the scenario. The authors give the first explanation in the background and the second in the methods, but they do not discuss whether/how the hypertension diagnosis could influence people's responses. A bigger concern is in the differences that the authors report as compared to the general Spanish population. They describe differences of up to 5 percentage points, but none of these seem to be meaningful even if they might be statistically significant. Overall, it's not clear to me that this manuscript adds anything meaningful beyond the results that are already reported from the authors' general survey of the Spanish population.

Another major question is regarding the differences between these results and the results on the Nayak et al. survey, particularly regarding relatively low levels of endorsement for verbal consent. Do the authors have any hypotheses to explain this difference? Why would the support for verbal consent be so much lower than general notification?

Some other specific concerns, which are likely addressable, include:

- The background section focuses on concerns about recruitment, which are of course important, but there is no mention of the ethical arguments for/against written consent. Some limited discussion of these arguments may be relevant.

- Line 73 refers to "only 76% of participants," which is not a fair characterization ("only" almost never means "76%"). Similarly, the description of the Kraft et al. study in lines 221-225 is written in a way that it mischaracterizes the results of that study. These examples raise a more general concern that other literature may not be cited carefully.

- While this manuscript focuses on a EU population, the authors discuss a fair amount of US-based data and refer to US trials, but they do not discuss or even mention the US regulations. It would help to provide a bit of regulatory background early on.
- The methods could benefit from some additional detail in this manuscript, rather than just citing to the other papers. Specifically, I would find it helpful to clarify how the scenarios were presented to participants - it is not clear, except for in one small line in the middle of the table that is easy to miss, that this was a hypothetical debate on a REC.

Finally, there were a number of places throughout the manuscript where the writing was quite unclear. The manuscript would benefit from thorough English grammatical review.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I recommend additional statistical review

**Quality of written English**
Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

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